ALASKA MEDICAID
PHARMACY AND THERAPEUTICS COMMITTEE

Location of Meeting
Frontier Building, 3601 C Street, Room 880/890

MINUTES OF
January 28, 2005
8:00 a.m.

Committee Members Present:
Terry K. Babb
Marvin Bergeson
Michael Boothe (late arrival)
Heidi Brainerd
Richard E. Brodsky
Robert H. Carlson
Kelly C. Conright (late arrival)
Jeffrey G. Demain
Traci Gale (telephonic, late arrival)
Arthur S. Hansen
R. Duane Hopson
Ronald Keller
Diane Liljegren (telephonic)
Ronald J. Miller
Janice L. Stables
George Stransky
Alexander H. vonHafften (late arrival)
Trish D. White (telephonic)

Committee Members Absent:
Thomas K. Hunt
Gregory R. Polston
Sherrie Richey

Others Present:
David Campana

I. CALL TO ORDER:

Chairman Brodsky called the meeting to order at 8:00 a.m.

II. ROLL CALL:

The roll call was taken and a quorum was present.

III. PUBLIC COMMENTS:

There were no public comments.

IV. RE-REVIEW ACE INHIBITORS (DIURETIC COMBINATIONS & CALCIUM CHANNEL BLOCKER COMBINATIONS)

Public Comments:

Andrew Weis, regional scientific associate director for Novartis Pharmaceuticals, discussed Lotrel. This is the only combination product featuring the most widely used, latest generation dihydropyridine calcium channel blockers, Amlodipine and Benazepril. JNC-VII found that one-third of hypertensive patients was controlled on their present medications, which left two-thirds of the patients non-controlled. JNC-VII also stated that most MI hypertensive patients would require two or more anti-hypertensive medications to achieve their blood pressure goals. The key to patient adherence is convenience, flexibility and a well-documented safety profile of the agents available for treatment. Previous patient behavior studies have indicated that multiple doses and multiple drug regimens are not conducive to patient adherence. Lotrel is dosed once daily and is available in three dosing strengths. We have filed for the FDA approval for two additional dosing strengths. Lotrel's components reach across a variety of special considerations in the treatment of hypertension, particularly with respect to hard to treat, diabetic and elderly patients. There are no significant effects from this combination in glucose levels, lipids, heart rate or demographic factors such as age, race and gender that can cause difficulties in treating patients to their blood pressure goals. The economic advantage of a combination product is twofold. There are no additional dispensing fees when patients using for add on therapy when patients who are presently on either Amlodipine or Benazepril therapy are added to the other. There is no additional co-pay for the patient. Being once a day, Lotrel is convenient and flexible. Lotrel has proven tolerability in a wide variety of patient groups. Lotrel is a combination anti-hypertensive product that may inherently enhance patient adherence through convenience, flexibility, and a well-documented safety profile and tolerability profile.

Ashesh Gandhi, Wyeth Pharmaceuticals, discussed Altace. Altace is the only ACE Inhibitor approved by the FDA to reduce the risk of stroke, MI or CB death in high risk patients 55 years of age or older. This indication was based on the results of the HOPE study, which demonstrated that Ramipril significantly reduced the primary composite endpoints of stroke, MI and CB in high-risk patients. Ramipril significantly reduced the risk of each of the individual endpoints of stroke, MI and CV (cardio vascular) death. The secondary endpoint of total mortality was also reduced significantly with Ramipril in the HOPE trial. These results have not been duplicated in any other major ACE Inhibitor clinical outcome trials. There are no head-to-head comparison trials of ACE Inhibitors, but there have been two observational studies. The first study showed that Ramipril treatment was independently associated with significantly lower hospital mortality and a lower rate of non-fatal major coronary and vascular events compared to other ACE Inhibitors. The second study demonstrated that mortality rates in the first year after acute MI was significantly lower with Ramipril compared to Enalapril, Fosinopril, Captopril, Quinapril and Perindopril. The cost effectiveness of Ramipril from the HOPE data has also been reported in several studies. In terms of safety, like all other ACE Inhibitors, Ramipril has a black box warning on use in pregnancy. Common adverse events associated with Ramipril include cough, dizziness and symptomatic hypertension. The robustness of the HOPE and Micro-HOPE trials have not been duplicated in any of the

other major ACE Inhibitor outcome trials. The other outcome trials demonstrated a reduction in the primary composite endpoint, but none of them have shown a reduction in each of the major individual endpoints.

P&T Committee Discussion:

Terry Babb noted that whatever products were preferred, the corresponding hydroclorothiazide combination product would be included. Over the last year there has been a 98% utilization of preferred agents within this class. Mr. Babb reviewed last year's discussion of ACE Inhibitors. The HOPE and EUROPA trials were reviewed. Captopril and its specific pharmacology parameters and its ability to be titrated was discussed and considered to be an important feature. Ramipril was a preferred agent based on the suggested reduction of cardiovascular risk in the HOPE trial. All other ACE Inhibitors were determined to be interchangeable. More information is coming out about the HOPE, EUROPA and PEACE trials in terms of tissue ACE effects or whether there is a specific benefit of Ramipril or other products in preventing cardiovascular risks. The PEACE (trandolapril) trial that was an add-on to already intensive therapy. People were on antiplatelets, beta-blockers and lipid lowering agents significantly more than in the HOPE trial. The Trandolapril, which is a tissue ACE product, showed no benefit and no significant difference in cardiovascular death, non-fatal MI, coronary artery bypass surgery or angioplasty. The PEACE trial differs from the HOPE and EUROPA trials, most notably because the patients were at a much lower risk. The summary data on hypertension, recent MI, heart failure, diabetic and non-diabetic nephropathy there are several agents within this class that have been shown to be equivalent. There are no head-to-head trials on the high cardiovascular risk. Ramipril is the only ACE Inhibitor to reduce all cause mortality, but Enalapril, Perindopril and Ramipril reduce major cardiovascular events in patients with coronary artery disease. The specialists, Dr. Gitomer, Dr. Schnellbaecher and Dr. Sapin, are strong proponents of Lisinopril. Dr. Gitomer feels that Lisinopril can be used in 90% of his patients. Dr. Schnellbaecher and Dr. Sapin use it exclusively. Dr. Gitomer is an advocate of Ramipril at 10 milligrams per day specific to its use in the HOPE study, which is patients 55 years of age or older that are subject to evidence of vascular disease, diabetes plus one other cardiovascular risk factor. Dr. Schnellbaecher and Dr. Sapin do not feel Ramipril needs to be a preferred agent. They appreciate the results of the HOPE trial, but feel it was more of a blood pressure lowering trial and the addition can be explained by a class effect. Captopril has nice pharmocology that allow it to be titrated, but it cannot be dosed once a day. Fosinopril is eliminated through dual mechanisms, so in renal dysfunction it does not need to be dose adjusted, which is different from others in the class. Lisinopril does not require hepatic activation and therefore should be considered the best choice for patients with severe hepatic dysfunction. A paper by the VA talks about opening the Ramipril capsules and sprinkling the contents on applesauce, so there is some flexibility in that product.

Heidi Brainerd said pediatricians mostly used Lisinopril.

Chairman Brodsky noted that last year the ACE Inhibitors were deemed a class effect, but Ramipril, based on the HOPE trial, and Captopril was added to the preferred drug list. He discussed Ramipril and whether it should remain on the list. The cardiologist expert

at last year's meeting recommended adding Ramipril based on the HOPE trial, but now many people feel it is more of a class effect for ACE Inhibitors.

In response to Jeffrey Demain, Terry Babb said less than 10% of last year's prescriptions were for Ramipril whereas 70% were for Lisinopril.

In response to Alexander vonHafften, Terry Babb said not all of the generics were included on the preferred drug list last year. The generic of Monopril, which does not need to be adjusted in rental dysfunction, was not a preferred agent for exclusivity issues. The committee has since decided that all the generics would be available for this class.

MARVIN BERGESON MOVED THAT THE ACE INHIBITORS WERE EQUIVALENT. SECONDED BY ALEXANDER vonHAFFTEN. CHAIRMAN BRODSKY CALLED FOR A VOTE ON THE MOTION. MOTION PASSED UNANIMOUSLY.

Chairman Brodsky noted that Michael Boothe, Kelly Conright and Alexander vonHafften had joined the meeting.

Terry Babb discussed the ACEI/Calcium Channel Blocker Combinations. This classification was not reviewed last year, although the components of the combinations were reviewed. There are three available brands. They are not indicated for the initial treatment of hypertension, but replacing the individual components once the patient has gone through titration. Lotrel dominates the entire class. The impact we had in terms of Lotrel being a non-preferred drug was a dramatic decrease in the utilization, which has gone down 67%. An article written in November/December of 2003 looked at adherence and noted patients using the combination drug, instead of two individual products, had less frequent medical care follow-ups. Dr. Schnellbaecher and Dr. Sapin value the use of multi anti-hypertensives and recognize the JNC-VII guidelines in reaching goal using two or three products. They do not use these combination products. Dr. Gitomer uses Lotrel exclusively. The components of Benazepril, Enalapril and Trandolapril are class effects. The difference is in the calcium channel blocker products. Amlodipine has virtually no drug interactions. Whereas Felodipine has significant CYP453 inhibitor interactions and Verapamil have numerous drug interactions.

George Stransky said he asked his internist at Providence Hospital, Dr. Makin, about combination products and he used them, because they cost less for the patient.

Robert Carlson said there were different tiers of pricing and co-pay amounts so a combination drug could be less, but not necessarily.

Chairman Brodsky pointed out that if the cost of the medication was much higher that might outweigh the prescribing fee costs of multiple medications. Patient compliance might be better with one medication versus multiple medicines, but some people avoid combination products, because they want to make sure they have the right mix of medications.

Terry Babb noted that if the co-pay amount was an issue for a patient, they did not have to pay it.

Dave Campana discussed the advantage of using a combination drug, which included better adherence, one dispensing fee and the recipient only has to pay one co-pay amount.

Heidi Brainerd said the Med Box Program is a service where pharmacies provide patients with individual medication regimes in unit ready-to-go packages to aid compliance and reduce confusion. They are filled in weekly increments and the state reimburses weekly dispensing fees for the preparation of these packages.

Chairman Brodsky said any medication that was not included on the preferred drug list could be prescribed using the medical necessity clause.

In response to Robert Carlson, Terry Babb said they did not have a specific recommendation on how to handle combination products.

Dave Campana said the combination products were currently non-preferred and required the statement of medical necessity. We are continuing to pay for a certain amount of combination products so it might be useful to take bids on them and have at least one of the products on the preferred drug list.

In response to George Stransky, Dave Campana said they could put a stipulation on the combination products that they would only be added to the preferred drug list if the price bids came in within a certain price range.

Arthur Hansen pointed out that the committee had selected drugs for the preferred drug list based on the benefits of the drug and not the prices. If a combination product works, it should be available on the preferred drug list.

Jeffrey Demain noted that 98% of the prescriptions written last year were within the approved preferred drug list and only 2% were medically necessary. Of the three experts, only one said he used the combination product for certain cases.

Terry Babb said the 98% adherence to the preferred drug list applied to the ACE Inhibitors. However, the preferred drug list has been widely accepted by the prescribing community overall.

In response to Marvin Bergeson, Terry Babb said there were 50-60 prescriptions written each month for these combination products.

Robert Carlson felt the committee should consider the individual drugs in the class and not deal with combination products unless First Health or the state felt there was an advantage to it.

JEFFREY DEMAIN MOVED TO CONTINUE THE PREFERRED DRUG LIST AS DEVELOPED LAST YEAR AND NOT PREFER ANY OF THE ACEI/CALCIUM CHANNEL BLOCKER COMBINATIONS. SECONDED BY

MARVIN BERGESON. CHAIRMAN BRODSKY CALLED FOR DISCUSSION ON THE MOTION. HEARING NONE, HE CALLED FOR A VOTE ON THE MOTION. MOTION PASSED WITH DR. STRANSKY OPPOSED.

V. RE-REVIEW BETA-BLOCKERS

Public Comments:

Mark Lattimore, medical information scientist for AstraZeneca, discussed Toprol XL. The MERIT-HF trial was a double blind placebo controlled study of Toprol XL conducted in 14 countries including the United States. It randomized approximately 4,000 patients with ejection fractions less than .40 in NYHA class 2-4 heart failure attributable to edema, hypertension or cardiomyopathy. The primary endpoints for the MERIT-HF trial were death plus hospitalization from any cause timed to the first event. There was a 19% reduction, which is highly significant. The other primary endpoint was death from any cause. This resulted in a 34% decrease. The secondary endpoints were sudden death and death from worsening heart failure. Sudden death decreased 41% and death from worsening heart failure decreased 49%. On this basis, adding Toprol XL to standard heart failure therapy will prevent about 700 out of 10,000 patients with heart failure from dying over the subsequent two years. Hospitalizations due to cardiovascular disease will drop nearly 1,500 over the same time period. The American Heart Journal published a recent article based on the MERIT-HF trial that specifically looked at diabetic patients. The risk for diabetic patients being hospitalized for heart failure is 76% more than that of patients without diabetes. This study showed that there is a 37% drop in hospitalizations of diabetic patients on Toprol XL and a 35% drop in hospitalizations in the non-diabetic group. The COMET study using Carvedilol did not use Toprol XL. It compared Carvedilol with immediate release Toprol at a dose of only 50 milligrams BID, which many felt was too low. Toprol XL does not have the traumatic peaks and troughs that immediate release preparations have, which can mean fewer side effects. Toprol XL has become the number one branded drug of cardiologists.

Randy Beckman, GlaxoSmithKline, discussed Carvedilol. Carvedilol is the only adrenergic blocking agent that blocks beta-1, beta-2 and alpha-1 receptors. It is the only FDA approved agent that is indicated in all stages of heart failure. The most recent clinical trial was a comparative trial of Carvedilol versus Metoprolol in the diabetic hypertensive patient looking at cardiovascular risk factors. It clearly demonstrated that Carvedilol was neutral as far as A1C levels. There was an increase in Metoprolol A1C levels. Looking at components of metabolic syndrome, Carvedilol improved its insulin sensitivity, microalbuminuria and total lipids. In the side effect profile, the two groups were identical except in two areas. In the Metoprolol group there was a greater number of worsening patients with diabetic control and a greater number of bradycardic patients. Coreg is the only FDA approved agent in post-MI patient with LVD, demonstrating a 22% reduction in mortality. Carvedilol is the only agent that has a mortality claim in heart failure. Evidence based medicine has clearly demonstrated the benefit of Carvedilol. The doses selected in the COMET trial were based on heart rate reduction and the heart rate reductions were comparable. In the COMET trial there was a 17% reduction in all cause mortality, 20% reduction in cardiovascular mortality, a 19% reduction in sudden death, a 67% reduction in stroke and a 22% reduction in the

development of type-two diabetes. Carvedilol is unique as an adrenergic blocking agent and has many of the indications, most recently in diabetic hypertensive patients.

Dr. Andrezej Maciejewski discussed Carvedilol, which was introduced into the U.S. market about seven years ago. In European countries, it is already in generic form and has been used for many years. Carvedilol links three components: alpha blocking, beta blocking and antioxidant. Alpha blocking reduces peripheral resistance in addition to beta blocking the heart, so we get a relaxation of the heart, treatment of diastolic dysfunction, improving performance and remodeling of the heart against reduced resistance. A pure beta-blocker would only work on the heart and would sometimes increase peripheral resistance. Carvedilol keeps a diabetic patient neutral. The GEMINI study showed diabetic patients using Carvedilol had fewer problems with glucose control.

P&T Committee Discussion:

Terry Babb said there were 13 beta-blocker products, five of which were branded. Their effects on various adrenergic receptors best classify beta-blockers. Some have membrane stabilizing activity and others have intrinsic sympathomimetic activity. We are currently at 96% utilization of preferred agents in this classification. Last year the discussions centered on the treatment of heart failure. We talked about the three products that have been shown to dramatically effect the outcome of heart failure: Bisoprolol, Coreg and Toprol. Bisoprolol, the generic of Zebeta, does not have an indication for heart failure in the United States, although it does in Europe and has been used for many years. Coreg and Toprol, particularly Toprol XL, have the indications for heart failure. Dr. Brodsky had noted last year that the local cardiology group was strongly in favor of Carvedilol. The GEMINI trial showed that Coreg had favorable effects on surrogate markers associated with diabetes, neutral effects on glycemic control, decreased insulin resistance and a decreased progression to microalbuminuria. The Oregon Evidence-based Practice Center summary data indicates that several products have demonstrated benefits with chronic stable angina, recent MI and hypertension. There is an ongoing debate regarding heart failure and the benefits of Carvedilol, the long acting form of Metoprolol and Bisoprolol. Dr. Gitomer said he exclusively uses Atenolol for hypertensive. He uses both Toprol XL and Coreg for the treatment of heart failure patients and has a slight preference towards Toprol XL. He believes Coreg's mechanism of action is significantly different and should be discussed as a separate classification. The cardiologists utilized less expensive products for the treatment of hypertension including Atenolol, Metoprolol and Labetalol. They reserve the Toprol XL and Coreg for the treatment of heart failure. The cardiologists prefer Coreg and have about 70% of their patients using Coreg instead of Toprol. In a letter received from the Alaska Heart Institute, they said they favor retaining both Coreg and Toprol as preferred agents. Coreg should be taken with food to slow absorption. Sotalol, both betapace and betapace AF, has a different pregnancy category. Propanolol can be used in children.

In response to Marvin Bergeson, Terry Babb did not feel the beta-blockers could be subdivided, because we pool with seven other states and they do not do that. However, that may be something that the pool could consider.

MARVIN BERGESON MOVED TO DECLARE A CLASS EFFECT, BUT ADD TOPROL AND COREG TO THE PREFERRED DRUG LIST. SECONDED BY RONALD KELLER. CHAIRMAN BRODSKY CALLED FOR DISCUSSION ON THE MOTION.

In response to Jeffrey Demain, Terry Babb said the utilization of the preferred drugs in this category was 96%.

In response to Janice Stables, Terry Babb said the committee had not discussed how the preferred drug list would effect the prescription writing in the beta-blocker category last year. One out of three beta-blocker prescriptions were for Coreg or Toprol. We can address that issue through a DUR Committee to develop criteria to insure that the more expensive products are being used only when appropriate.

Dave Campana said the DUR Committee oversees the utilization to verify its appropriateness for the indications. We look at individual patient profiles to determine whether or not there are drug interactions or if the utilization appears to be appropriate. If there are concerns, we do interventions with the providers listed on the profile.

Terry Babb said the DUR Committee also develops criteria for prior authorization to insure drugs are being properly used and not abused. We could require a prior authorization process when a physician prescribes higher priced beta-blockers to insure they are being properly used.

Chairman Brodsky said the utilization pattern for the beta-blockers seems to be inappropriate, because there is such a large selection of Carvedilol and Toprol XL, which should be reserved for patients with heart failure and hypertension. In some cases, a less expensive beta-blocker is effective.

In response to Alexander vonHafften, Terry Babb said once a company is on the preferred drug list, they use that to advantage. Some physicians might think Coreg or Toprol is the better agent, although less severe conditions could be better treated with less expensive alternatives.

Kelly Conright felt the prior authorization process would be too onerous. She suggested specifying on the preferred drug list that the drug was preferred for CHF only.

Terry Babb said Nevada required physicians to put ICD-9 codes on certain prescriptions. They bypass the prior authorization process, but add another level beyond just writing medically necessary. They are asked to justify the prescription based on an ICD-9 code that the patient has heart failure.

Marvin Bergeson wondered if another group might be using these medications for metabolic syndrome because of its affects on diabetes.

George Stransky suggested adding a statement to the preferred drug list that the medicine is for treatment of congestive heart failure in conjunction with hypertension.

Michale Boothe felt the committee was straying from their charge by considering finances instead of the pharmacology and therapeutic aspects of the drugs.

Diane Liljegren felt the committee was making assumptions that the increased usage was due to physicians using the drugs incorrectly. It might be due to the fact that more doctors are appropriately treating CHF. She strongly objected to any kind of edits, except including some informational data.

Jeffrey Demain said Carvedilol has therapeutic actions that are not seen in the other medications and should be a separate agent. Toprol XL needs more discussion as to whether it has significant benefits over the other beta-blockers.

Terry Babb said the MERIT-HF trial showed Carvedilol was effective in the treatment of heart failure. In addition, it has the beta-1 selectivity. For patients with respiratory disorders or those who may benefit from additional rate control, Toprol is favored over Carvedilol.

In response to Janice Stables, Dave Campana said the patients presently using Carvedilol and Toprol could be grandfathered in and future prescriptions could have additional restrictions.

In response to Ronald Miller, Chairman Brodsky said prescriptions for Carvedilol and Toprol have increased since they were added to the preferred drug list. These are drugs that are clearly an advance over the other beta-blockers for a particular set of patients.

MARVIN BERGESON AMENDED THE MOTION TO DECLARE A CLASS EFFECT, INCLUDE TOPROL XL AND CARVEDILOL, AND ADD EDUCATIONAL MATERIAL ON THE WEBSITE AND THE SHEET ON THE INDICATION OF THOSE TWO SPECIFIC DRUGS. SECONDED BY RONALD KELLER. CHAIRMAN BRODSKY CALLED FOR A VOTE ON THE MOTION AS AMENDED. MOTION PASSED UNANIMOUSLY.

VI. RE-REVIEW DIHYDROPYRIDINE CALCIUM CHANNEL BLOCKERS

Public Comments:

Mike Estoup, a clinical education consultant for Pfizer, discussed Amlodipine. After last year's review, the committee came to the conclusion that Amlodipine was the best agent for Alaskan residents. Since the initial review, additional data has been published that supports this decision. Head to head data exists for Amlodipine with the diuretics, ACE Inhibitors and angiotensin receptor blockers. The data consistently demonstrates Amlodipine to be as safe and effective as the other agents. The AL-HEFT study was the largest hypertensive study ever conducted and enrolled over 40,000 patients at moderate cardiovascular disease risk. Amlodipine was found to be comparable to Chlorthalidone with respect to the primary endpoint of fatal coronary heart disease and non-fatal MI. It also had the lowest rate of stroke in comparison to Chlorthalidone and the ACE Inhibitor Lisinopril. The ACE Inhibitor demonstrated a 15% higher rate of stroke and a 10% higher incidence of combined cardiovascular events than Chlorthalidone. The PRAISE-I

and PRAISE-II studies demonstrated the safety and effectiveness of Amlodipine in patients with class three and four heart failure. No other agent in this class has this type of data. The VALUE trial, sponsored by Novartis, was a head-to-head comparison between Amlodipine and Valsartan. VALUE enrolled over 15,000 patients, greater than the age of 50 with treated or untreated hypertension. It randomized patients to receive one or the other therapies and titrated the dose to a blood pressure of less than 140 over 90. 32% of the population had diabetes, 42% were female. There was no difference in the primary endpoint of composite cardiac morbidity or mortality between the two groups, although more pronounced blood pressure reduction and a significant reduction in fatal and non-fatal MIs were observed in the Amlodipine treated patients. The CAMELOT study is the most recently published study. This study evaluated the effectiveness of Amlodipine and Enalopril, compared to placebo, in preventing major cardiovascular events in normal-tensive patients as defined in JNC-VI standards, with established coronary disease. The findings were very similar to that in VALUE. Other key elements with respect to Amlodipine include the absence of significant drug interactions and a low incidence of side effects, features that few agents in any class possess. Not to be overlooked is the long half-life of Amlodipine conferring true 24-hour blood pressure control. This confers the ability to split or crush the formulation without concerns of altering the tablet matrix, which are important characteristics that allow the drug to be administered through feeding tubes and dosed with food. No other agent in this class has the abundance of favorable characteristics and the vast level of clinical evidence as Amlodipine. Amlodipine is the preferred dihydropyridine calcium channel blocker as designated by the Oregon Health Sciences Evidence-based Practice Center and previous decisions by state PDL committees in Oregon, Washington and Alaska.

P&T Committee Discussion

Terry Babb said there were seven dihydropyridine calcium channel blocker products, four of which were brand only. Our utilization over the last year is 98%. Last year's discussion was that although all dihydropyridine calcium channel blockers were equally efficacious, Amlodipine was identified as having better tolerability, flexibility and easiest to use in this class. We had a significant discussion about both Amlodipine and Plendil, which was only available as brand and has since gone generic, as the two dihydropyridine calcium channel blockers that have been proven to be safe and effective in the treatment of hypertension in patients with systolic heart failure as well. He agreed with Dr. Estoup's discussion regarding the significant changes that have occurred. The conclusion from the Oregon Evidence-based Practice Center on the treatment of hypertension and chronic stable angina was that there are several products within this class that can be used. There is consistent evidence of equivalence with one exception. Treatment of hypertension in patients with systolic dysfunction only, Amlodipine and Felodipine have had no significant effects, either negative or positive, on all cause mortality and combined fatal and non-fatal cardiovascular events. Dr. Gitomer has concerns with worsening proteinuria when using the long acting form of Nifedipine. He acknowledges the efficacy of both Amlodipine and Felodipine to lower blood pressure, however he uses Amlodipine almost exclusively due to four significant issues: the long half-life, the lack of drug interactions, and the flexibility with dosing. Dr. Schnellbaecher and Dr. Sapin generally use long-acting Nifedipine, but they readily will use Amlodipine if the patient has systolic heart failure requiring a significant blood pressure effect or when patients

have difficulty tolerating the long-acting Nifedipine. Most of the positive effects favor Amlodipine due to its long half-life, the once daily formulation that has the ability to be crushed and used for patient that have swallowing difficulties, its labeled indication for use in children 6-17 years of age, and the lack of drug interactions. The negative distinguishing features include the interaction with grapefruit juice is significant with Nifedipine, Nicardipine, Felodipine, Nisoldipine and others. Last year the committee had decided the class was equally efficacious, but Amlodipine needed to be on the preferred drug list.

In response to Robert Carlson, Terry Babb said the JNC-VII guidelines recommend certain classes of drugs to be used as first line agents. We see a predominance of those types of medication, but calcium channel blockers is not one of those agents although they clearly have a place.

MARVIN BERGESON MOVED THAT NO CHANGE SHOULD BE MADE TO THE PREFERRED DRUG LIST FOR THE DIHYDROPYRIDINE CALCIUM CHANNEL BLOCKERS CLASS. SECONDED BY JEFFREY DEMAIN. CHAIRMAN BRODSKY CALLED FOR DISCUSSION ON THE MOTION. HEARING NONE, HE CALLED FOR A VOTE ON THE MOTION. MOTION PASSED UNANIMOUSLY.

VII. RE-REVIEW NON-DIHYDROPYRIDINE CALCIUM CHANNEL BLOCKERS AND PHENYLALKYLAMINE NON-DIHYDROPYRIDINE CALCIUM CHANNEL BLOCKERS

Non-Dihydropyridine calcium channel blockers and phenylalkylamine non-dihydropyridine calcium channel blockers were combined into one discussion.

Public Comments:

Dr. Andrzej Maciejewski discussed Cardizem LA. The non-dihydropyridine calcium channel blockers have less edema, are potent when it comes to blood pressure control and are better tolerated in a majority of patients. The formulation of Cardizem LA is unique, because of its delivery system. This is supported by blood pressure measurements using 24-hour ambulatory devices. 80% or more of the hypertensive patients have dual behavioral blood pressure, which peaks early in the morning and then slowly drops. That behavior is correlated with higher mortality, stroke and other complications. Cardizem LA has fewer side effects, because it releases most of the medication during the early hours to bring the blood pressure down and has less effect in the late evening. Cardizem LA lowers the heart rate, to some degree. If the patient has a conduction problem, Cardizem LA may unmask that, but those patients will typically require a pacemaker anyway. Cardizem LA is approved up to 540 milligrams per day, but that is not necessarily a maximum dose. The dose response curve indicates that higher doses are probably safe and efficacious. He felt Cardizem LA should be added to the preferred drug list.

P&T Committee Discussion

Terry Babb said the non-dihydropyridine calcium channel blockers and the phenylalkylamine non-dihydropyridine calcium channel blockers would be combined into one discussion. There are four products, Diltiazem, long acting Diltiazem, Verapamil and long acting Verapamil. All are available generically, except for some of the more recent branded products. The utilization in this class is at 96%. In last year's discussion, we reviewed and determined that all non-dihydropyridine calcium channel blockers were equivalent. There have not been any significant changes since last year. The OSHU summary for hypertension, chronic stable angina and chronic AF suggests there is a class effect. Dr. Gitomer does not use these products very often, but when he does then he favors the long acting Diltiazem branded product. Dr. Schnellbaecher and Dr. Sapin support the generic formulations of both long acting Diltiazem and Verapamil as preferred. From a cardiologist standpoint, they do not believe that any of the branded products have evidence to support any benefit with dosage formulations such as Covera-HS, Verelan PM and Diltiazem LA and feel they should be non-preferred. There are numerous drug interactions in both the Diltiazem and Verapamil camp, although significantly more with Verapamil. Cardizem LA is the only long acting Diltiazem product labeled to be given either in the morning or evening. It has less ionotropic activity and more effect on the system vascular resistance as well as some minor effects on myocardium, but not nearly to the degree as the Verapamil products. The Verapamil products can be useful in treating some arrhythmic conditions. The CONVINCE trial showed no benefit in outcome. It may have had some effect on blood pressure, but it did not show superiority in outcomes using the chronotropic (ph) agent versus the standard extended release product.

JANICE STABLES MOVED THAT NO CHANGE SHOULD BE MADE TO THE PREFERRED DRUG LIST FOR THE NON-DIHYDROPYRIDINE CALCIUM CHANNEL BLOCKERS CLASS. SECONDED BY GEORGE STRANSKY. CHAIRMAN BRODSKY CALLED FOR DISCUSSION ON THE MOTION.

In response to Alexander vonHafften, Terry Babb said they reviewed all the calcium channel blockers together and the dihydropyridine is only about 2% of that particular class. If you look at these specifically, 33% of the prescriptions are written for Cardizem LA, reflecting an increase of about 50%.

CHAIRMAN BRODSKY CALLED FOR A VOTE ON THE MOTION. MOTION PASSED UNANIMOUSLY.

VIII. RE-REVIEW FIBRIC ACID DERIVATIVES

Public Comments

There were no public comments.

P&T Committee Discussion

Terry Babb said the utilization in this class was at 72%, which increased from 46%. Last year we determined that Gemfibrozil should be on the preferred drug list. There are no significant changes from last year's discussions and no OSHU summary available. We

included the VHA Pharmacy Benefits Management Strategic Health Care Group and the Medical Advisory Panel summary data information. They looked at the question of safety between the products. They said no firm conclusions could be drawn between differences in serious adverse events between Gemfibrozil and Fenofibrate when combined with statins. As a result, the combination could not be routinely recommended. However, they did go on to say that in mixed dyslipidemias there was some support that these should be used in combination for particular patients, especially if they are at risk for coronary heart disease events. We did not discuss this with Dr. Gitomer. Dr. Schnellbaecher did not use this class of drugs enough to provide a recommendation. Dr. Sapin supports Tricor, because there is favorable safety data, especially when used with high dose statins. Gemfibrozil has an outcome indication for reducing coronary heart disease risk and positive effects on HDL. Tricor has significantly greater effects on LDL. The impact of this is somewhat questionable, because the patients will be on a statin as well. Gemfibrozil has negative features specific to drug interactions, specifically with agents that are commonly used in these types of patients, such as anti-diabetic medications. It has been shown that use of Gemfibrozil with a statin leads to an increased risk of rhabdomyolysis. Gemfibrozil has to be dosed twice a day specific to meals. Tricor does not have those concerns. Fenofibrate has an issue with hyperhomocysteinemia and the recommendation is to supplement patients with a significant amount of folic acid to prevent that issue. Last year Gemfibrozil was added to the preferred drug list.

In response to Jeffrey Demain, Terry Babb said when the committee says there is a class effect, any changes to the preferred drug list will be delayed until April when the new bids come out so we can get a full year of use for those particular agents.

The committee discussed what had transpired at last year's meeting. Dave Campana said they discussed the fact that Tricor had fewer drug interactions.

RONALD KELLER MOVED THAT THE DRUGS WERE EQUIVALENT. SECONDED BY JEFFREY DEMAIN. CHAIRMAN BRODSKY CALLED FOR DISCUSSION ON THE MOTION. HEARING NONE, HE CALLED FOR A VOTE ON THE MOTION. MOTION PASSED UNANIMOUSLY.

The committee discussed miscellaneous topics.

Changes to the Committee

Chairman Brodsky noted that Charlene Hampton has resigned from the committee and this would be Dr. Hansen last meeting. The new members will be appointed and introduced at the next meeting.

Approval of Meeting Minutes

Chairman Brodsky said the meeting minutes of October 29, 2004 and November 19, 2004 needed to be approved. Alexander vonHafften said he had not had time to review the meeting minutes and asked to have this action deferred to the next meeting. Diane Liljegren noted that there were numerous typos in the minutes. Jeffrey Demain noted

that the typos were predominately in the names of drugs and did not change the meaning of the minutes. Dave Campana said he could correct the typos and send the minutes out with the next meeting's information.

Dave Campana referred to the meeting minutes of November 19, 2004, page 7 of 21. The second line in the last paragraph should read "The mechanism of action for the proton pump inhibitors is to prevent production of acid in the stomach." Paragraph six on page 9 of 21 was confusing. Terry Babb said the intent of that sentence was once somebody bids on a particular product, it always maintains at least that level and never goes higher. They have an opportunity to bid more aggressively, meaning on subsequent years they can add lower BIDS (prices), but it can never go up. Terry Babb suggested "Prices can be modified in the three year period, but they can never be increased." Paragraph four on page 18 of 21 should read "In response to Janice Stables, Dave Campana said Dr. Tomera indicated that the patch was nice for compliance issues, especially in a caregiver situation, because it could be applied twice weekly."

GEORGE STRANSKY MOVED TO APPROVE THE MEETING MINUTES OF NOVEMBER 19, 2004 AS AMENDED. SECONDED BY ARTHUR HANSEN. CHAIRMAN BRODSKY CALLED FOR DISCUSSION ON THE MOTION. HEARING NONE, HE CALLED FOR A VOTE ON THE MOTION. MOTION PASSED UNANIMOUSLY.

Changes to the Bylaws

Dave Campana reviewed the changes to the procedure for public testimony, which needed to be changed in the bylaws on page 3. An unidentified male suggested changing "local physicians" to "local health care providers."

GEORGE STRANSKY MOVED TO APPROVE THE CHANGES TO THE BYLAWS. SECONDED BY ALEXANDER vonHAFFTEN. CHAIRMAN BRODSKY CALLED FOR DISCUSSION ON THE MOTION. HEARING NONE, HE CALLED FOR A VOTE ON THE MOTION. MOTION PASSED UNANIMOUSLY.

IX. REVIEW OF P&T COMMITTEE PROCEDURES

Chairman Brodsky said he and Terry Babb updated the P&T Committee procedures utilizing the updated public input. The changes included the format of the public testimony, distribution of information, forwarding letters to the committee and other things that were discussed. Dave Campana said the new procedures would be published on the Internet. George Stransky suggested changing "local physicians" to "local health care providers" on page 2.

GEORGE STRANSKY MOVED APPROVAL OF THE UPDATED P&T COMMITTEE PROCEDURES AS AMENDED. SECONDED BY JEFFREY DEMAIN. CHAIRMAN BRODSKY CALLED FOR DISCUSSION ON THE MOTION. HEARING NONE, HE CALLED FOR A VOTE ON THE MOTION. MOTION PASSED UNANIMOUSLY.

Terry Babb said an administrative meeting was held the day before the P&T Committee meeting to discuss issues of concern or new drugs that could potentially impact previous decisions. If a new drug did not offer any advantages to what was currently reviewed, it received a standard review. He discussed several new drugs that would undergo standard reviews and be added to the drug class review.

Chairman Brodsky said a breakthrough drug could be reviewed before the re-review of the class. The commissioner's office decided that the mental health drugs would not be implemented at this time. He requested having the commissioner attend the next meeting to explain why this decision was made. Dave Campana said the entire class of mental health drugs was about one-third of the budget. Adding the opiates would bring it up to about 40% of the budget.

Alexander vonHafften pointed out that there might be other issues that the P&T Committee was unaware of that went into the commission's decision. He felt the P&T Committee needed clarification on their role in the psychiatric medications.

Arthur Hansen said the Mental Health Board had misconceptions of what the P&T Committee was doing and feed misinformation to people. The executive director said they did not have any input, although I have offered to listen to their concerns. The Mental Health Board consists of consumers or family members of consumers and they are petrified of having their medications cut off.

DIANE LILJEGREN MOVED THAT THE COMMISSIONER BE INVITED TO THE NEXT P&T COMMITTEE MEETING TO DISCUSS THE ISSUE OF THE MENTAL HEALTH DRUGS. SECONDED BY RONALD MILLER. CHAIRMAN BRODSKY CALLED FOR A VOTE ON THE MOTION. MOTION PASSED UNANIMOUSLY.

Terry Babb said one of the previous classes reviewed was the high potency statins. After reviewing the information, the committee determined they were therapeutically interchangeable or a class effect. After going to the NMPI pool, Simvastatin and Resuvistatin were selected. Atorvastatin was non-preferred. The hard edits were made on December 1, 2004. Dr. David Graham spoke to Congress about five drug classes with safety concerns and Rosuvastatin was one of them. He referenced four piece of information including the website rosuvastatininformation.com and the pink sheet newsletter. The FDA's current view is there is no greater risk for muscle injury with cholesterol lowering Crestor compared to the other statins. There was a recent fatal death that some felt was related rhabdomyolysis. His understanding was that it was more indicative of (indiscernible) malignant syndrome than rhabdomyolysis. After discussing the issue with Chairman Brodsky, it was decided that the committee should re-review the class at the next meeting.

The committee discussed the issue. Chairman Brodsky said a nephrologist had contacted him regarding Crestor. He felt the drug was harmful and should be removed from the preferred drug list. Terry Babb said he had reviewed the information and did not feel there was a problem, but the committee review the information and determine what their

next step should be. Chairman Brodsky suggested giving the committee time to review the information and discussing the issue at the next meeting. Terry Babb said other organizations that recently reviewed these classes came to the same conclusion as the P&T Committee.

The committee discussed what information they would like to review before discussing this issue at the next meeting. The committee asked for a medical letter and FDA med watch information. Robert Carlson suggested asking for information from other non-profit organizations that had a lot of consumer input.

In response to Alexander vonHafften, Terry Babb said Jeff Monahan from Nevada said they approved Rosuvastatin for their preferred drug list. In response to the negative information, they put a restriction on the 40-milligram dose. In a two month span, Alaska has had 650 prescriptions for Resuvistatin; less than 20 were for the 40-milligram dose. The committee could decide to restrict the 40-milligram dose.

Jeffrey Demain wondered if the committee should review all five of the drugs that were in question. Terry Babb noted that not all of the five drugs had been added to the preferred drug list.

The committee further discussed this issue and how the P&T Committee should handle the possible re-review. Arthur Hansen felt the entire class should be re-reviewed if there was a problem within the class. Marvin Bergeson felt the class should only be re-reviewed if the information indicated there was a major change. Jeffrey Demain felt the committee had a responsibility to insure the drugs on the preferred drug list were safe and effective. Michale Boothe felt the committee had a responsibility to base their opinions on science and not public opinion. Chairman Brodsky suggested reviewing the materials and then the committee could decide at the next meeting if they needed to re-review the class. George Stransky suggested distributing the information, having Terry Babb give a five-minute review of the information and then voting on whether the committee should re-review the class.

GEORGE STRANSKY MOVED THAT THE COMMITTEE RECEIVE THE INFORMATION, TERRY BABB PRESENT A SHORT REVIEW AND THEN A VOTE BE HELD TO DETERMINE IF THE COMMITTEE SHOULD RE-REVIEW THE CLASS. SECONDED BY RONALD KELLER. CHAIRMAN BRODSKY CALLED FOR DISCUSSION ON THE MOTION. HEARING NONE, HE CALLED FOR A VOTE ON THE MOTION. MOTION PASSED UNANIMOUSLY.

Chairman Brodsky noted that the March meeting would be cancelled, because a number of the members would not be available. The next meeting would be February 18, 2005.

The committee discussed holding meetings on a quarterly basis. Dave Campana said they would review the issue after the February, April and May meetings. No meetings would be held in the summer months.

GEORGE STRANSKY MOVED TO ADJOURN THE MEETING. SECONDED BY RONALD MILLER. CHAIRMAN BRODSKY CALLED FOR A VOTE ON THE MOTION. MOTION PASSED UNANIMOUSLY.

The meeting adjourned at 11:00 a.m.